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| 09/575,554 | 05/22/2000 | Brett P. Monia | ISPH-0463 | 1277 |

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| EXAMINER |
|---|
| FREDMAN, JEFFREY NORMAN |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1655 | 8 |

DATE MAILED: 11/15/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

| Application No. | Applicant(s) |
|---|---|
| 09/575,554 | Monia et al |
| **Examiner** | **Art Unit** |
| Jeffrey Fredman | 1655 |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) ☒ Responsive to communication(s) filed on *May 24, 2001* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

**Disposition of Claims**

4) ☒ Claim(s) *1 and 7-20* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1 and 7-20* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

**Application Papers**

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

## DETAILED ACTION

### *Double Patenting*

1. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

2. Claim 6 is rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 1 of prior U.S. Patent No. 5,872,242. This is a double patenting rejection.

3. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

4. Claims 1, 2, 5 and 7-23 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 5,576,208. Although the conflicting claims are not identical, they are not patentably distinct from each other because the species claims of U.S. Patent No. 5,576,208 anticipate the larger genus claims 1, 2, 5 and 7-23 of the current application. These species necessarily render the genus claim obvious since they fall directly within the scope of the genus claim.

5. Claims 1, 2, 5 and 7-23 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 5,582,986.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the species claims of U.S. Patent No. 5,582,986 anticipate the larger genus 1, 2, 5 and 7-23 of the current application. These species necessarily render the genus claim obvious since they fall directly within the scope of the genus claim.

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

***Claim Rejections - 35 USC § 112***

7. The rejection of claims 1-5 and 7-23 under 35 U.S.C. 112, first paragraph, is withdrawn in view of the amendment.

***Claim Rejections - 35 USC § 103***

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1 and 7-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bos, Daaka et al., Hall et al (Nucleic Acids Res. 13(14):5255-5268) and Saison-Behmoaras et al., each in view of Uhlmann et al., Agrawal et al. and Inoue et al., and further in view of Smith. Bos discloses antisense oligonucleotides to human H-ras and Ki-ras and to the specific regions of ras genes (codons 12 and 61) that are mutated in the activated forms of these genes (see Column 4, line 26 to Column 5, line 10). Bos teaches that the molecules of the invention may be labeled and used in methods to detect the activated forms of ras, by either hybridizing to single-stranded genomic DNA fragments or to RNA isolated from cells or tissue to be tested. Hall teaches the sequence of N-ras from which the specific antisense molecules are derived as well as the importance of the mutations at codons 12 and 61 (page 5256, and page 5264, figure 4). Daaka et al. teach antisense molecules to the translation initiation codon site of the H-ras gene and the use of the antisense molecules to inhibit H-ras expression in and the growth of transformed 3T3 cells.

Saison-Behmoaras et al. teach oligonucleotides that specifically hybridize to the codon 12 region of H-ras and methods of using the oligos to inhibit expression of the gene. Thus, the three primary references all provide teachings of oligonucleotides directed against the claimed regions of H-ras or Ki-ras and their use to inhibit expression of the gene and growth of transformed cells, or to detect the activated genes. The primary references do not teach oligos having phosphorothioate linkages, chimeric oligonucleotides containing runs of phosphodiester-linked oligodeoxynucleotides flanked by RNase H-resistant oligonucleotides, modifications to increase the affinity toward the target, the specific oligonucleotide sequences of the instant invention or the method of treating an animal by administering the oligonucleotides of the invention. Uhlmann et al. teach a wide variety of modifications to antisense oligonucleotide structures, including phosphorothioate backbone modifications and the use of 2'-modified ribonucleotides such as 2'-O-methyl nucleotides. Uhlmann et al. disclosed motivation for making oligos with these modifications to increase stability and decrease costs. They also disclosed that 2'-O-methyl modified oligonucleotides formed duplexes with RNA that were more thermostable than DNA-RNA hybrids, thus suggesting that 2'-O-methyl oligos had increased affinity for their RNA targets. Inoue et al. and Agrawal et al. each teach the RNase H sensitivity or resistance of duplexes formed from RNA and various modified oligonucleotides. Agrawal discloses that phosphodiester and phosphorothioate backbones confer sensitivity to RNase H, whereas oligos with methylphosphonate and some other backbone structures confer resistance to RNase H. Inoue et al. disclosed chimeric antisense oligonucleotides containing resistant 2'-O-methyl residues

flanking at least 4 deoxynucleotide residues. These molecules, after forming a duplex with complementary RNA, promoted specific cleavage by RNase H in the tetradeoxynucleotide region of the duplex. Smith et al. disclose the use of antisense oligonucleotides, with or without modified backbones, against oncogenes or genes that are differentially expressed in tumor cells, as a treatment for cancer. Thus, they disclose a method of treating cancer by administering appropriate antisense oligos to inhibit the growth of tumor cells or kill the tumor cells. Although the oligonucleotides that are claimed by specific sequence are not specifically disclosed in the art, the regions of the genes to which they are targeted are clearly taught in the art. The specific sequences would be derived by one of ordinary skill in the art making a variety of antisense oligonucleotides targeted at the taught regions. Thus, one of ordinary skill in the art would have known at the time the invention was made to modify the teachings of the primary references by making oligonucleotides that have modified backbones, stretches of deoxynucleotides that are sensitive to RNase H digestion and 2' modified ribose moieties as disclosed by Uhlmann et al., Agrawal et al. and Inoue et al., in order to obtain the advantages of increased stability, target affinity and target destruction taught by the secondary references. One of ordinary skill in the art would further have known to use the oligos in methods of preventing expression of the ras gene, inhibiting tumor cell growth and treating an animal having an activated ras gene, and in methods of detecting different forms of the ras gene, as suggested by the primary references and Smith for the obvious advantages of slowing or stopping tumor growth and diagnosing the presence or absence of activated forms of the ras gene, which are linked to cancer. Therefore, the invention

as a whole was *prima facie* obvious in the absence of evidence or secondary considerations to the contrary.

Further, Bos provides the requisite sequence information for Ki-ras. Hall provides the requisite sequence information for N-ras. Motivation is provided by several of these references. Saison-Behmoaras states "It has been found that 10-20% of human tumors have a mutation in one of the three ras genes (Ha-ras, Ki-ras, N-ras) leading to the production of p21 ras oncoproteins, which are thought to play an important role in the transformed phenotype (page 1111, column 1)". Here, Saison-Behmoaras discloses the equivalence of the three ras oncogenes and provides a strong and direct motivation to inactivate each of these genes, since they are found activated in 10-20% of human tumors. Saison-Behmoaras continues "In order to study the biological effects of ras expression in the context of molecular biology of ras-dependent pathway and to provide a rational basis for the development of antitumor drugs we are investigating the use of antisense oligonucleotides and their modified analogues, which upon hybridization to complementary mRNA sequences, interfere with translation and thus can be employed for sequence-specific control of gene expression. In an attempt to inhibit the expression of an oncogene, application of antisense oligonucleotides has proved to be a powerful tool (page 1111, column 1 to column 2)". This quote demonstrates that Saison-Behmoaras provides a motivation to utilize antisense oligonucleotides to achieve the goal, as noted above, of inactivation of ras oncogenes, since antisense oligonucleotides were known to be a powerful tool to interfere with translation and gene expression of the ras oncogenes and since the antisense oligonucleotides could provide a rational

basis for drug development. Further motivation is provided by Daaka, who states "The ras family of mammalian protooncogenes includes three members, termed Ha-ras, Ki-ras, and N-ras, that are likely to play a fundamental role in basic cellular functions based on their high degree of conservation throughout eukaryotic evolution (ref omitted). The amino acid sequence of the ras gene products all contain GTP-binding consensus regions and are thought to be localized to the inner surface of the plasma membrane (ref omitted). In mammals, ras proteins have been implicated in cellular proliferation (ref omitted) and terminal differentiation (ref omitted). Point mutations in ras oncogenes that alter the enzymatic properties and/or cause overexpression of the ras p21 oncoprotein may be causatively or closely linked ot the onset of some types of human tumors (refs omitted) (page 267, columns 1 and 2)." Daaka here also motivates the ordinary practitioner to inactivate mutated ras proteins, including any of the three equivalents, Ha-ras, Ki-ras or N-ras. Daaka also teaches the use of antisense methodologies to perform this inactivation (page 267, column 2 to page 268, column 1). Bos et al also motivates the inactivation of the ras oncogene, though Bos does not suggest an antisense mechanism " The human gene family consists of three members: the H-ras, K-ras and the N-ras gene (1) These genes code for related proteins of 21kD, which are located at the inner face of the cell membrane (36) and are thought to be involved in transducing signals from cell surface receptors to their intracellular targets (37). A significant portion of tumor cell lines and fresh tumor tissue has been found to possess an activated ras gene. Such genes are characterized by their ability to induce oncogenic transformation of mouse 3T3 cells. In most cases so far analyzed the activation is due to a point

mutation in the 12th or 61st codon of a ras gene resulting in a single amino acid substitution in the gene product (column 1, lines 14-26)".

These three references each note the linkage and potential causative nature of ras oncogenes with human tumors. Each reference discloses that three different, but functionally and structurally equivalent ras oncogenes termed Ha-ras, Ki-ras and N-ras are involved in human tumors. Saison-Behmoaras and Daaka explicitly motivate the inactivation of these proteins by antisense mechanisms to inhibit tumor formation and growth. These references thus provide explicit motivation for the ordinary practitioner to inactivate Ki-ras, Ha-ras and N-ras in order to inhibit tumor formation and growth.

***Response to Arguments***

10. Applicant's arguments filed May 24, 2001 have been fully considered but they are not persuasive.

The terminal disclaimer does not fully overcome the double patenting rejection because it only refers to the 5,872,242 patent and does not include the 5,576,208 and 5,582,986 patents.

Applicant presents a series of separate arguments detailing asserted missing pieces in each individual reference. In response to applicant's arguments against the references individually, one cannot show non-obviousness by attacking references individually where the rejections are based on combinations of references. *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). It is essential to recognize that this rejection is made as a combination of several different teachings. The examiner agrees

that a prima facie case requires motivation in the art, reasonable expectation of success and teaching of the claim limitations.

Applicant correctly notes that Bos does not teach antisense oligonucleotides to Ki-Ras, that Daaka and Saison-Behmoaras only exemplify antisense oligonucleotides to H-ras and that the remaining references do not mention Ki-ras. It is, however, the combination that provides the rejection. Bos provides the requisite sequence information for Ki-ras. Motivation is provided by several of these references. Saison-Behmoaras states "It has been found that 10-20% of human tumors have a mutation in one of the three ras genes (Ha-ras, Ki-ras, N-ras) leading to the production of p21 ras oncoproteins, which are thought to play an important role in the transformed phenotype (page 1111, column 1)". Here, Saison-Behmoaras discloses the equivalence of the three ras oncogenes and provides a strong and direct motivation to inactivate each of these genes, since they are found activated in 10-20% of human tumors. Saison-Behmoaras continues "In order to study the biological effects of ras expression in the context of molecular biology of ras-dependent pathway and to provide a rational basis for the development of antitumor drugs we are investigating the use of antisense oligonucleotides and their modified analogues, which upon hybridization to complementary mRNA sequences, interfere with translation and thus can be employed for sequence-specific control of gene expression. In an attempt to inhibit the expression of an oncogene, application of antisense oligonucleotides has proved to be a powerful tool (page 1111, column 1 to column 2)". This quote demonstrates that Saison-Behmoaras provides a motivation to utilize antisense oligonucleotides to achieve the goal,

as noted above, of inactivation of ras oncogenes, since antisense oligonucleotides were known to be a powerful tool to interfere with translation and gene expression of the ras oncogenes and since the antisense oligonucleotides could provide a rational basis for drug development. Further motivation is provided by Daaka, who states "The ras family of mammalian protooncogenes includes three members, termed Ha-ras, Ki-ras, and N-ras, that are likely to play a fundamental role in basic cellular functions based on their high degree of conservation throughout eukaryotic evolution (ref omitted). The amino acid sequence of the ras gene products all contain GTP-binding consensus regions and are thought to be localized to the inner surface of the plasma membrane (ref omitted). In mammals, ras proteins have been implicated in cellular proliferation (ref omitted) and terminal differentiation (ref omitted). Point mutations in ras oncogenes that alter the enzymatic properties and/or cause overexpression of the ras p21 oncoprotein may be causatively or closely linked ot the onset of some types of human tumors (refs omitted) (page 267, columns 1 and 2)." Daaka here also motivates the ordinary practitioner to inactivate mutated ras proteins, including any of the three equivalents, Ha-ras, Ki-ras or N-ras. Daaka also teaches the use of antisense methodologies to perform this inactivation (page 267, column 2 to page 268, column 1). Bos et al also motivates the inactivation of the ras oncogene, though Bos does not suggest an antisense mechanism " The human gene family consists of three members: the H-ras, K-ras and the N-ras gene (1) These genes code for related proteins of 21kD, which are located at the inner face of the cell membrane (36) and are thought to be involved in transducing signals from cell surface receptors to their intracellular targets (37). A significant portion of tumor

cell lines and fresh tumor tissue has been found to possess an activated ras gene. Such genes are characterized by their ability to induce oncogenic transformation of mouse 3T3 cells. In most cases so far analyzed the activation is due to a point mutation in the 12th or 61st codon of a ras gene resulting in a single amino acid substitution in the gene product (column 1, lines 14-26)". These three references each note the linkage and potential causative nature of ras oncogenes with human tumors. Each reference discloses that three different, but functionally and structurally equivalent ras oncogenes termed Ha-ras, Ki-ras and N-ras are involved in human tumors. Saison-Behmoaras and Daaka explicitly motivate the inactivation of these proteins by antisense mechanisms to inhibit tumor formation and growth. These references thus provide explicit motivation for the ordinary practitioner to inactivate Ki-ras in order to inhibit tumor formation and growth.

The references direct the practitioner to codon 12 and 61 mutations and the 5' or 3' UTR of Ki-ras because Saison-Behmoaras states "In the ras gene family, activation of the protooncogene to form the oncogene is due to point mutations, most often in the 12th and 61st codons (page 1111, column 2)". This statement is generic to all three ras gene family members, including Ki-ras. This statement also directs the ordinary practitioner to design antisense oligonucleotides at these two sites, which is completely constrained by the known sequence of Ki-ras. Given the teachings noted above for the equivalence of the three ras genes, an ordinary practitioner would have designed probes for each gene equivalent to known working probes. Daaka discloses, on page 272, column 1, working 5' UTR probes for Ha-ras, which would direct

the practitioner to design equivalent probes for Ki-ras. Ki-ras is known to be so identical to Ha-ras that they function identically and identical common mutations at codons 12 and 61 are responsible for aberrant function. Further motivation would be provided by Uhlmann, who states under the subheadings "Selection of effective target sequences" on page 576 that "As is evident from figure 47, a large number of target sequences are suitable for inhibiting gene expression. At the level of translation, these are the 5' non coding regions, the ribosome binding site, the translation start region, the coding region, and the 3' non translated region (page 576, column 1 paragraph 1)". Uhlmann explicitly directs the ordinary practitioner to the 5' UTR and the 3'UTR for selection of effective target sequences.

Applicant argues that the references do not provide a reasonable expectation of success for the antisense probes. Applicant argues that the references teach that testing of oligonucleotides will have to be performed for each gene. If applicant is attempting to argue that a secondary consideration such as unexpected results exists which would overcome the rejection, then factual evidence should be presented to support the argument that the results are unexpected. With regard to Applicant's argument on expectation of success, the MPEP 2143.02 states "The prior art can be modified or combined to reject claims as prima facie obvious as long as there is a reasonable expectation of success." Two references which relate to Ha-ras support the rejection on this point. Daaka, a reference in which antisense oligonucleotides were synthesized based on secondary structure considerations and tested against a closely related protein, Ha-ras, demonstrates that all three tested oligonucleotides exhibited antisense inhibitory function. This

evidence supports a reasonable expectation of success, since 100% of the tested oligonucleotides met the test requirements. Saison-Behmoaras also demonstrates that antisense oligonucleotides have a reasonable expectation of success. Saison-Behmoaras shows 7 different H-ras specific antisense oligonucleotides (see page 1112, figure 1) of which 6 demonstrate acceptable antisense activity. This 85% success rate also supports the reasonable expectation of success. Applicant has provided no evidence for the allegation that synthesis of antisense oligonucleotides would lack a reasonable expectation of success. Further, Daaka, on page 267, column 1 to page 267, column 2, details eleven papers discussing successful uses of antisense oligonucleotides including three targeted against Ha-Ras. . The argument that some testing may be required to identify functional oligonucleotides does not challenge the reasonable expectation of success. Applicant has not provided evidence or sound scientific reasons against a reasonable expectation that genes with 80% nucleotide identity and so many other similiarities would differ in sequence requirements for antisense oligonucleotides.

***Conclusion***

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman, Ph.D. whose telephone number is (703) 308-6568.

The examiner is normally in the office between the hours of 6:30 a.m. and 4:00 p.m., and telephone calls either in the early morning or the afternoon are most likely to find the examiner in the office. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission via the P.T.O. Fax Center located in Crystal Mall 1. The CM1 Fax Center numbers for Technology Center 1600 are either (703) 305-3014 or (703) 308-4242. Please note that the faxing of such papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

**Jeffrey Fredman**
**Primary Patent Examiner**
**Art Unit 1655**

November 14, 2001